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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/535,508

12/16/2005

Roberto Angelo Motterlini

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EXAMINER

SOROUGH, ALI

ART UNIT

PAPER NUMBER

1617

MAIL DATE

DELIVERY MODE

08/17/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/535,508	Applicant(s) MOTTERLINI ET AL.	
	Examiner ALI SOROUGH	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 June 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-10 and 16-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-10 and 16-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>04222010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Acknowledgement of Receipt

Applicant's response filed on 06/07/2010 to the Office Action mailed on 01/05/2010 is acknowledged.

Status of the Claims

Claims 1, 3-10, 16-20, 22 and 23 are currently amended. Therefore, claims 1, 3-10 and 16-23 are currently pending examination for patentability.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. The rejection of claims 1, 3-10, and 16-23 under 35 U.S.C. 103(a) as being unpatentable over Oeltgen et al. (US Patent 6645938 B2, Published 11/11/2003, Filed 01/10/2001) in view of Motterlini et al. (Carbon Monoxide-releasing Molecules

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Characterization of Biochemical and Vascular Activities, Circulation Research,
Published 02/08/2002) **is maintained**.

Applicant Claims

Applicant claims a method of treatment of an extracorporeal organ or isolated organ comprising contacting said organ with a composition comprising a metal carbonyl compound wherein the metal carbonyl compound makes available carbon monoxide to limit post-ischemic damage to said organ.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Oeltgen et al. teach methods for "Protection against ischemia and reperfusion injury". (See title). "Tissues deprived of blood and oxygen undergo ischemic necrosis or infarction with possible irreversible organ damage. In some circumstances, however, such as during cardiac surgery, it is desirable to interrupt the normal myocardial contractions (cardioplegia) and actually induce ischemia." (See column 1, Lines 14-18). "The same problems also occur during organ storage for cardiac transplant, under which there are time constraints due to the limits of myocardial preservation." (See column 1, Lines 45-48). "In one embodiment, a method of protecting against ischemia and reperfusion injury in a mammal is disclosed. An effective concentration of compound D SED ID NO:1 is administered to the mammal in a pharmaceutically acceptable formulation ... prior to ... substantially concurrent with ... during ... or post-ischemia. " (See column 2, Lines 17-25). "The invention is also directed to a method to

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prevent damage to an isolated organ, for example, a heart for transplant. The isolated organ is exposed to a preservative solution containing an effective amount of compound-D SED ID NO: 1." (See column 2, Lines 28-32).

***Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)***

Oeltgen et al. does not teach a preservative solution comprising a metal carbonyl compound which makes available carbon monoxide. This deficiency is cured by the teachings of Motterlini et al.

Motterlini et al. teaches $[\text{Ru}(\text{CO})_3\text{Cl}_2]_2$ freshly dissolved in DMSO (see page 19, column 2, paragraph 3) was added consecutively to aortic rings (see page 21, column 1, paragraph 2) which were isolated from male Lewis rats (see page 19, column 1, paragraph 5). Motterlini et al. teaches that $[\text{Ru}(\text{CO})_3\text{Cl}_2]_2$ freshly dissolved in DMSO releases CO into the solution. (See page 19, column 2, Paragraph 3). Motterlini et al. teaches that upon administration of light CO is released from Pentacarbonyl by the mechanism of photodissociation. (See page 19, column 2, Paragraph 3). Motterlini et al. teach that "transition metal carbonyls could be utilized for therapeutic delivery of CO to alleviate vascular- and immuno-related dysfunctions." (See abstract). Further, Motterlini et al. teach that CO releasing compounds have been found to be pivotal in the defensive system against ischemia-reperfusion damage. (See page 17, column 1, paragraph 1).

***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Oeltgen et al. with Montterlini et al. One would have been motivated to do so because Montterlini et al. teaches that the transition metal carbonyls taught are useful for defense against ischemia-reperfusion damage and therefore, adding such a compound to the solution taught by Oeltgen would enhance the protective activity of the solution. For the foregoing reasons, the instant method would have been obvious to one of ordinary skill in the art at the time of the instant invention.

Response to Applicant's Arguments

Applicant argues that Motterlini et al. does not teach or suggest that CO releasing compounds are pivotal in the defensive system against ischemia-reperfusion damage but rather teach HO-1 has such an activity. Applicant's argument has been fully considered but found not to be persuasive. It is the Examiners position that the Motterlini et al. teach that HO-1 results in the formation of CO and that it is pivotal in the protection of ischemic-reperfusion damage. Motterlini et al. further teach that the HO derived CO has cytoprotective activity. (See page 17, column 1, paragraph 1). It is the Examiners position that these teachings indicate CO-releasing molecules in general have ischemia-reperfusion protective activity. Further, it is the Examiners position that the teaching of Motterlini et al. shows that it is CO compound that has the protective activity against ischemic-reperfusion damage along with other disease states. It is the

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Examiners position that this observation is what lead Motterlini et al. to study the activity of CO-releasing carbonyl compounds.

Applicant also argues that there is no motivation in Oeltgen et al. to either modify the peptide compound used in the preservative or use compounds other than the peptide compound. Furthermore, applicant argues that even there was some motivation to substitute the peptide compound with another compound, one of ordinary skill would not be motivated to use a carbon monoxide-releasing molecule as taught by Motterlini et al. Applicants arguments have been fully considered but found not be persuasive. Motterlini et al. teach that carbon monoxide-releasing compounds "represents a pivotal inducible defensive system against stressful stimuli, including ... ischemia-reperfusion damage ..." (See page 17, column 1, paragraph 1). Therefore, it is the Examiners position that one of ordinary skill in the art would be motivated to combine the carbon monoxide-releasing molecules of Motterlini et al. with the composition taught by Oeltgen et al. in order to give an additive effect of both the peptide molecule and the carbon monoxide-releasing molecule in protecting against ischemia-reperfusion damage.

Applicant finally argues that the instant invention is not related to a combination of compounds. Applicant's argument has been fully considered but found not to be persuasive. Applicant's claims are directed to a "method comprising" which reads on methods utilizing one or more agents including compound-D as taught by Oeltgen et al. For the foregoing reasons, the instant rejection of claims 1, 3-10, and 16-23 under 35 U.S.C. 103(a) is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ali Soroush whose telephone number is (571) 272-9925. The examiner can normally be reached on Monday through Thursday 8:30am to 5:00pm E.S.T.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

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information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ali Soroush
Patent Examiner
Art Unit: 1616

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616